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(54) DNA mutagenesis by random fragmentation and reassembly for antibody production

(57) The present invention provides a population of polynucleotides resulting from shuffling sequences from substrate polynucleotides encoding antibody chains, whereby the population of polynucleotides comprises recombinant polynucleotides encoding antibody chains having different combinations of heavy chain CDRs and/or light chain CDRs than are encoded by the substrate polynucleotides. Such a population of polynucleotides may be employed to provide an antibody display library.

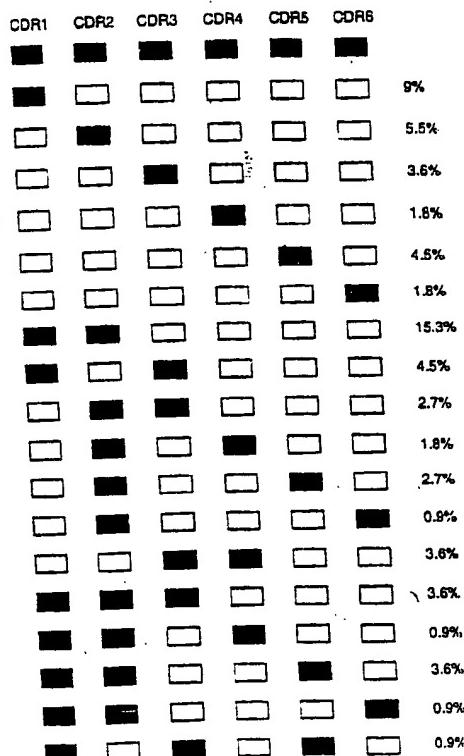


Figure 7



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EUROPEAN SEARCH REPORT

Application Number
EP 01 10 0962

DOCUMENTS CONSIDERED TO BE RELEVANT									
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)						
X	BALINT R F ET AL: "ANTIBODY ENGINEERING BY PARSIMONIOUS MUTAGENESIS" GENE, vol. 137, no. 1, 27 December 1993 (1993-12-27), pages 109-118, XP002031537 * page 111, right-hand column, line 32 - page 112, left-hand column, line 35 *	15-26	C12N15/10 C12N15/12 C07K16/18 C12Q1/68						
X	WO 91 15581 A (CREA ROBERTO) 17 October 1991 (1991-10-17) * claims 1-42; figure 1; example 1 *	15-26							
A	R.I. NEAR: "Gene conversion of immunoglobulin variable regions in mutagenesis cassettes by replacement PCR mutagenesis" BIOTECHNIQUES, vol. 12, no. 1, 1992, pages 88-97, XP002090391 NATICK, MA, US * the whole document *								
A	J.D. MARKS ET AL.: "By-passing immunization: Building high affinity human antibodies by chain shuffling" NATURE BIOTECHNOLOGY, vol. 10, no. 7, July 1992 (1992-07), pages 779-783, XP002092023 NATURE PUBL. CO., NEW YORK, US * the whole document *	-/-	C12N C12Q C07K						
<p>The present search report has been drawn up for all claims</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">Place of search</td> <td style="width: 33%;">Date of completion of the search</td> <td style="width: 34%;">Examiner</td> </tr> <tr> <td>THE HAGUE</td> <td>12 March 2001</td> <td>Hornig, H</td> </tr> </table>				Place of search	Date of completion of the search	Examiner	THE HAGUE	12 March 2001	Hornig, H
Place of search	Date of completion of the search	Examiner							
THE HAGUE	12 March 2001	Hornig, H							
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document							
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Application Number
EP 01 10 0962

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
A	S. DELAGRAVE AND D.C. YOUVAN: "Searching sequence space to engineer proteins: Exponential ensemble mutagenesis" NATURE BIOTECHNOLOGY, vol. 11, no. 11, December 1993 (1993-12), pages 1548-1552, XP002162579 NATURE PUBL. CO., NEW YORK, US * the whole document * ---		
A	A.R. OLIPHANT ET AL.: "Cloning of random-sequence oligonucleotides" GENE, vol. 44, 1986, pages 177-183, XP002162580 ELSEVIER SCIENCE PUBLISHERS, B.V., AMSTERDAM, NL; * the whole document *		
A	STEMMER WILLEM P C ET AL: "Selection of an active single chain Fv antibody from a protein linker library prepared by enzymatic inverse PCR." BIOTECHNIQUES, vol. 14, no. 2, 1993, pages 256-265, XP002162581 ISSN: 0736-6205 * the whole document *		TECHNICAL FIELDS SEARCHED (Int.Cl.7)
A	WO 93 12228 A (PASTEUR INSTITUT) 24 June 1993 (1993-06-24) * the whole document *		
<p>The present search report has been drawn up for all claims</p>			
Place of search THE HAGUE	Date of completion of the search 12 March 2001	Examiner Hornig, H	
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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ON EUROPEAN PATENT APPLICATION NO.**

EP 01 10 0962

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The members are as contained in the European Patent Office EDP file on
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12-03-2001

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9115581	A	17-10-1991	AT 126535 T AU 653152 B AU 7741891 A CA 2079802 A DE 69112207 D DE 69112207 T EP 0527809 A ES 2078518 T KR 173131 B US 5830650 A US 5798208 A	15-09-1995 22-09-1994 30-10-1991 06-10-1991 21-09-1995 28-03-1996 24-02-1993 16-12-1995 01-02-1999 03-11-1998 25-08-1998
WO 9312228	A	24-06-1993	FR 2685004 A CA 2125192 A EP 0618965 A JP 7504086 T US 5756323 A	18-06-1993 24-06-1993 12-10-1994 11-05-1995 26-05-1998

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82